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09/735,056	12/11/2000	Leonard Katz	4952.US.C1	4609

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EXAMINER

MOORE, WILLIAM W

ART UNIT

PAPER NUMBER

1652

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DATE MAILED: 06/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/735,056

Applicant(s)

KATZ ET AL.

Examiner

William W. Moore

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 March 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 57-83 is/are pending in the application.
- 4a) Of the above claim(s) 63-71 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 57-62 and 72-83 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 27 March 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|----------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Election/Restriction

Applicant's election **with** traverse of the inventions of Groups I and II, comprising claims 57, 58 and 72-83, in part, and claims 59-62 in their entirety, at page 6 of Paper No. 10, filed March 27, 2003, is acknowledged. The grounds for traversal is that joint examination of further methods of claims 63-71 together with elected methods of claims 59-62 would entail no "significant additional burden on the examiner". This is not found persuasive because the restriction requirement stated in Paper No. 7 mailed September 27, 2003, specified the separate nature of the different polyketide synthase activities that are modified in inventions of Groups I-VI and explained that a search required for any of the distinct classes of enzymatic modifications would be distinct and would not be required for other searches. Where multiple, distinct, searches are required, the search burden is undue, thus the requirement as to restriction among Groups directed to distinct species of enzymatic modifications is still deemed proper and is therefore made FINAL.

Response to Amendment

Applicant's Amendment B, Paper No. 10 filed March 27, 2003, has been entered. The substitute specification and amendments of claims 57, 73, 77 and 81-83 of Paper No. 10 overcome the objections of record of the elected claims as well as the rejection of record of claims 59-62, 72-75, 77, 78, 82 and 83 under the first paragraph of 35 U.S.C. §112 for lack of an adequate written description. Applicant's arguments at pages 11 and 12 of Paper No. 10 are persuasive in overcoming the rejection of record of claims 57-62, 72-74, 77, 78, 82 and 83 herein under the first paragraph of 35 U.S.C. §112 for lack of enablement. While the amendments to claims 57, 81 and 82 remove the bases for the rejection of record of claims 57-62 and 72-83 herein under the second paragraph of 35 U.S.C. §112, a new ground of rejection under the second paragraph is necessitated

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by the amendments to claims 57, 81 and 82 of Paper No. 10 and is stated below. It is noted that claims 57 and 58 were not amended to limit their scope to the elected species of enzymatic modifications and also noted that claims 63-71 drawn to non-elected species of enzymatic modifications remain in the application.

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Substitute Specification

The substitute specification submitted with Paper No. 10 on March 27, 2003 is APPROVED. The corrected, substitute, Drawing Figure 44 received on March 27, 2003, is acceptable. Examples 1-16 and 27-44, and Figure 3, of Applicant's priority application serial No. 07/642,734 - now U.S. Patent No. 5,824,513 - are present in the substitute specification as Examples 29-62 and Figure 44 and disclose the preparation of products supporting the practice of elected methods for biosynthesis of specific polyketides wherein β -ketoreductase, dehydratase, or enoylreductase domains of a polyketide synthase [PCS] are altered. It is agreed that the disclosure at page 19 of the substitute specification are commensurate with disclosures at column 4, lines 63-66, of U.S. Patent No. 5,824,513.

It is noted that both the preliminary amendment to page 1, line 1, of the specification, submitted with Paper No. 6 filed December 11, 2000, with the specification, and the continuing data information now appearing beneath the title at page 1 of the substitute specification, state an erroneous serial number for Applicant's earliest priority document and erroneously state that the application was abandoned. Instead, the application serial No. 07/642,734 was issued as U.S. Patent No. 5,824,513.

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Abstract

The abstract of the disclosure is objected to because no new, replacement, abstract was submitted with Paper No. 10 and because the abstract filed December 11, 2000, remains the abstract but no longer describes an invention of the subject matter of the elected claims. Correction or replacement is required. See MPEP § 608.01(b). It is

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noted that a corrected or replacement abstract cannot have a length exceeding 150 words and must be in a clear, concise, narrative form that avoids the use of phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc., as well phraseology such as "means" and "said".

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Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. §112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10 Claims 57-62 and 72-83 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

15 This is a new ground of rejection necessitated by the amendments of Paper No. 10 to claims 57, 81 and 82. Claim 57 is indefinite in reciting, in its clause 2, "a polyketide synthase domain encoding for an enzymatic activity", and in reciting, in its clause 3, "introducing one or more specified changes into said polyketide synthase domain resulting in an altered DNA sequence". The terms of clause 2 confound the intended subject matter and are technically unsound where a domain is recognized in the art as a polypeptide or peptide structure, composed of amino acids, and to be incapable of encoding anything because it can neither be replicated, transcribed, nor translated. Clause 20 3 of the claim also confounds the intended subject matter because altering a domain of a polyketide synthase polypeptide cannot result in altering any DNA sequence; instead Applicant's disclosed - and intended - process does the obverse, altering a native DNA sequence in order to change the structure, the amino acid sequence, of a specific domain, either deleting it in whole or in part or adding a domain where one had not previously 25 been present in the primary structure of the polyketide synthase. Claims 58-62 and 72-83 are included in the rejection of claim 57 because they depend therefrom but fail to correct its indefinite description. Claims 81 and 82 are independently rejected because they are indefinite in reciting, respectively, "protein" and "proteins" where Applicant

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actually intends, the disclosure requires, and claim 57 provides antecedent basis only for a particular kind of protein: a polyketide synthase.

To avoid multiple amendments of the independent claim 57, to provide scientifically sound terminology, and to better describe the intended subject matter of methods elected

5 by Applicant, the following format is suggested for the claim:

A method for directing the biosynthesis of a specific polyketide analog by genetic manipulation of a polyketide-producing microorganism, wherein the method comprises the steps of:

10 (1) isolating a DNA sequence from a polyketide-producing microorganism encoding a polyketide synthase polypeptide comprising one or more domains providing enzymatic activities that support polyketide biosynthesis;

(2) identifying one or more regions of the DNA sequence encoding specific domains within the polyketide synthase polypeptide;

15 (3) altering the DNA sequence encoding the polyketide synthase polypeptide by either or both of,

20 (i) disrupting the DNA sequence encoding the polyketide synthase in one or more regions encoding a domain providing a β -carbonyl processing enzymatic activity selected from the group consisting of a β -ketoreductase, dehydratase, or enoylreductase, the disruption resulting in inactivation of said enzymatic activity in polyketide biosynthesis, and,

25 (ii) inserting within the DNA sequence encoding the polyketide synthase one or more DNA sequences encoding a domain providing a β -carbonyl processing enzymatic activity selected from the group consisting of a β -ketoreductase, dehydratase, or enoylreductase, the insertion resulting in the addition of said enzymatic activity in polyketide biosynthesis;

(4) transforming a polyketide-producing microorganism with the altered polyketide synthase-encoding DNA sequence to replace its native polyketide synthase-encoding DNA sequence of the microorganism;

30 (5) culturing the transformed microorganism in conditions suitable for the expression of the altered polyketide synthase and the biosynthesis of a specific polyketide analog by the altered polyketide synthase; and,

(6) isolating the specific polyketide analog from the cultured cells or the culture medium.

35 It is noted that adopting such a format for claim 57 would render claims 58, 60 and 62 redundant, permitting their cancellation, and would also require amendments of claims 81 and 82 in order that they may conform to the revised recitation of claim 58.

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Conclusion

Applicant's amendment necessitated the new grounds of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

5 A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not
10 mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

15 Any inquiry concerning this communication or earlier communications from the examiner should be directed to William W. Moore whose telephone number is 703.308.0583. The examiner can normally be reached between 9:00AM and 5:30PM EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached at 703.308.3804. The fax
20 phone numbers for the organization where this application or proceeding is assigned are 703.308.4242 for regular communications and 703.308.0294 for After Final communications. The examiner's direct fax phone number is 703.746.3169. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703.308.0196.

25 William W. Moore
May 27, 2003



PONNATHAPU ACHUTAMURTHY
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